hematologic recovery was observed in most patients, with values of ANC >500 and platelet >20,000 being reached at 13 and 16 days, respectively. Cardiac toxicity was monitored by echocardiogram. All patients demonstrated a normal left ventricular ejection fraction (LVEF) prior to receiving the conditioning regimen. There were no deaths attributable to heart failure. A significant decline in LVEF developed in only one patient who was over age 60 with underlying diabetes and hypertension. Ninety-four percent of patients survived the first 100 days following transplant. To date, 7 patients are alive and in remission at 2 to 7 years since disease onset, with no patients lost to follow-up. The 3-year failure-free and overall survival are 44% and 55%, respectively. We conclude that high dose mitoxantrone and melphalan is an effective and easily administered conditioning regimen with a low risk of significant cardiac toxicity despite prior treatment with anthracycline based chemotherapy, and thus is a safe regimen for APBSCT in adults with AML.

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### COMPARISON OF FIXED DOSE (6 MG) PEGFILGRASTIM AND DAILY FILGRASTIM TO ACCELERATE HEMOPOIETIC RECOVERY AFTER AUTOLOGOUS STEM CELL TRANSPLANTATION (ASCT)

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High dose therapy plus Autologous Stem Cell Transplantation (ASCT) is a milestone treatment program for most hematologic malignancies. ASCO guidelines recommend the use of granulocyte colony stimulating factors (G-CSF) in the post-infusion phase, to shorten the period of severe neutropenia and reduce the related risk of life-threatening infections. Thus, daily subcutaneous injections of G-CSF (filgrastim/lenograstim) at 5 μg/kg dose until ANC > 500/μl are routinely administered from day +1 following ASCT, in order to accelerate hematopoietic recovery and to avoid neutropenic complications. Pegfilgrastim, a novel long-acting recombinant G-CSF, has been shown to have similar efficacy when compared to G-CSF for chemotherapy-induced neutropenia, but little is known about its use in the ASCT setting. We used a 6 mg fixed dose Pegfilgrastim on day +4 following ASCT in 47 patients (23 male/24 female; median age 56 years; range 22–70 years) with multiple myeloma (26 pts) and relapsed or refractory Hodgkin's and non- Hodgkin's lymphoma (21 pts). Patients received peripheral $CD34^+$ stem cells (median number $4.4 \times 10^6$/kg; range 1.8–1.8) harvested after mobilizing chemotherapy (cytoxan, vinorelbine/cytoxan, R-IEV, IGEV, R-ICE) and G-CSF. Standard conditioning regimens (HD-Melphalan or BEAM) were used. Engraftment results were compared to those from a historical control group of 182 patients (median age 56 years; range 16–74 years) who had received HD-Melphalan or BEAM and ASCT (median $CD34^+$ cells $7.6 \times 10^6$/kg; range 1.8–14.6) supported by G-CSF (5 μg/kg/day from day +1 until ANC > 500/μl). Median number of days to ANC > 500/μl were comparable between the Pegfilgrastim (10, range 8–15) and G-CSF (11, range 7–22) groups, as well as the median number of days to PLT > 20,000/μl (Pegfilgrastim = 12, range 9–20 vs G-CSF = 12, range 7–29). Overall infectious rates, including FUO and documented infections, were of 48% and 39% for Pegfilgrastim and G-CSF groups, respectively ($P$ = NS). Median number of days on iv antibiotics were 0 (range 0–18) and 6 (range 0–13) for the Pegfilgrastim and G-CSF groups, respectively. No significant differences in the incidence of bone pain, intensity of transfusion support, and length of hospital stay were documented between the two groups. These data indicate that a fixed 6 mg single-dose of Pegfilgrastim is safe and effective to accelerate engraftment after ASCT. No significant differences with G-CSF were apparent as to engraftment times and overall infectious complications.

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### PREDICTABILITY OF PRETRANSPLANT INTRAVENOUS BUSULFAN (IVBU) PK DATA IN ACHIEVING TARGETED IVBU AUC'S DURING CONDITIONING IN AUTO BMT

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Eight adult patients with hematological malignancies were enrolled in a phase I IVBU dose-escalation trial in autologous BMT conditioning. All patients received four daily doses of IVBU followed by 2 days of cyclophosphamide (CP) with amifostine cytoprotection. There were 4 planned cohorts of patients with an increasing targeted IVBU AUC of 20% in each subsequent cohort. The targeted average daily AUC range for IVBU in cohort 1 was 4400–5280 uMol*min/dose (mean 4800), the AUC range commonly achieved by single daily doses of 3.2 mg/kg/day. PK data from 6 time points over 5 hours was obtained from an IVBU test dose of 0.4 mg/kg administered to patients 7 to 21 days prior to conditioning. Test dose data was used to achieve the targeted IVBU AUC for conditioning doses 1 and 2. IVBU PK data was also collected around conditioning doses 1 and 3 at 7 points over 20 hours. If the targeted daily AUC range was not achieved based on the IVBU PK data for dose 1, IVBU doses were adjusted to correct the AUC during days 3 and 4 IVBU was measured in plasma samples using a validated gas chromatography method. Acetaminophen and metronidazole were held during all IVBU administration. Fungal prophylaxis was the same during IVBU test and conditioning doses. Patients received phenytoin for seizure prophylaxis. All PK data followed expected pharmacokinetic behavior. In cohort no. 1, test dose PK data resulted in achieving the targeted AUC for 3 of 5 (60%), but in none of the 3 patients in cohort no. #2 based on first IVBU conditioning dose PK results. The test dose PK data resulted in a lower than targeted AUC in 5 patients. Of these 5 patients, 4 achieved the targeted 4-day AUC after dose adjustments. Hepatic veno-occlusive disease was diagnosed in 2 patients in cohort no. 2 after IVBU doses were increased to obtain the targeted mean 4-day AUC. The study was closed. Utilizing PK data based on a small pretransplant IVBU test dose with limited blood sampling of up to 5 hours did not accurately predict conditioning AUCs, especially when higher targeted AUCs were desired. PK data from first dose IVBU conditioning dose was more predictive of later IVBU conditioning AUCs. This suggests that conditions during the test dose as proposed in this study did not accurately reflect those of conditioning and/or that a higher test dose with more comprehensive blood sampling might be more predictive in estimating IVBU dose when single daily busulfan is administered with targeting strategy (Table1).

**Table 1.** *IVBU PK Data*

| Patient no. | Desired IVBU Conditioning AUC Range | Dose 1 AUC | Dose 3 AUC | Ave 4-Day Daily AUC |
|---|---|---|---|---|
| 1 | 4400–5280 | 3558 | 8590 | 6074 |
| 2 | 4400–5280 | 4864 | 4853 | 4858 |
| 3 | 4400–5280 | 5152 | 6232 | 5692 |
| 4 | 4400–5280 | 4771 | 4870 | 4820 |
| 5 | 4400–5280 | 4223 | 5358 | 4790 |
| 6 | 5281–6340 | 4034 | 6858 | 5446 |
| 7 | 5281–6340 | 4905 | 6586 | 5745 |
| 8 | 5281–6340 | 4051 | 6207 | 5129 |

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### TANDEM HIGH DOSE THERAPY WITH HEMATOPOIETIC PROGENITOR CELL RESCUE IN CHILDREN WITH HIGH-RISK SOLID TUMORS

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A major advance in the treatment of high-risk patients with solid tumors has been to intensify therapy. We hypothesize that the use of tandem high dose chemotherapy followed by stem cell rescue